

REMARKS:

Reconsideration and allowance in view of the foregoing amendments and the following remarks are requested. By this amendment, Applicants have amended claims 1, 2, 20, 21, and 26-31. New claims 32-33 have been added to define further embodiments of the invention. No new matter is added.

Claims 26-31 were rejected under 35 U.S.C. §101 as being non-statutory “use” claims. Applicants submit that claims 26-31 have been rewritten as “method” claims, thus obviating the rejection under 35 U.S.C. §101.

Claims 20 and 21 were rejected under 35 U.S.C. §112, second paragraph, for not particularly pointing out and distinctly claiming the subject matter which the applicant regards as the invention. The Examiner asserts that there is insufficient antecedent basis for the limitation “the sequence of the nucleic acid or of the nucleic acid double strand” in claims 20 and 21. Furthermore, the Examiner asserts that it is not clear whether the nucleic acid cited in claims 20 and 21 refer to the nucleic acids being synthesized or the nucleic acids bound to the surface prior to addition of nucleotide building blocks. Claims 20 and 21 have been amended to correct the antecedent basis by deleting “nucleic acid double strand” and to clarify that that the nucleic acids being referred to are the nucleic acids that are generated. Claim 1 has been amended to relate to a method for preparing single stranded nucleic acids and is supported by the disclosure on page 24, lines 21-23 of the specification.

Claims 1-31 were rejected under 35 U.S.C. §102(b) as being anticipated by Chetverin et al. (U.S. 6,322,971). Chetverin et al. is directed to arrays comprising immobilized oligonucleotides that hybridize to nucleic acids to bind, sort, and manipulate DNA or RNA strands in a sample (see Chetverin paragraph bridging columns 4 and 5). The disclosure of Chetverin is directed to methods of producing a copy of an unknown DNA sequence by digesting a DNA sample with restriction endonuclease, restoring the ends of each fragment, generating priming sequences, melting the double stranded DNA apart, hybridizing a DNA strand to a terminal sequence binding sorting array on a support, washing to remove unhybridized strands, incubating with DNA polymerase, consequently generating a complementary copy of the hybridized DNA strand by extension of the 3' end of the oligonucleotide to which the strand is bound. The array is then vigorously washed to remove the original DNA strands and all other material not covalently bound to the surface (see Chetverin column 16, lines 22-46). Thus, the unknown sample is the template. The array-bound oligonucleotides are used as primers and they are extended. The method of Chetverin produces an oligonucleotide that is bound to the support that contains a complementary copy of the unknown DNA sample.

Thus, the method of Chetverin comprises:

Step 1: Generation of a partial copy of a nucleic acid mixture on the array

Step 2: Deleting the nucleic acid mixture from the array

Step 3: Copying and optionally amplifying the carrier-bound sequences as partial copies of the original nucleic acid mixture.

Conversely, the present invention is characterized by the following features:

- A method for the production of synthetic single or double stranded nucleic acids (de novo). Chetverin discloses generation of partial copies of the added nucleic acid mixture.
- The nucleic acid fragments are detached from the carrier. In Chetverin, the extended fragments remain on the carrier.
- The complete identity of the product has to be defined/known at the beginning of the method steps (because the sequences present on the support are complementary to the nucleic acids that the practitioner wants to prepare). In Chetverin, partial copies of the known or unknown added nucleic acid mixture are formed on the carrier- thus, the carrier is the generated copy of the nucleic acid mixture.

The present claims are directed to a method of producing a plurality of nucleic acids on a support by immobilizing a nucleic acid sequence which is known and is complementary to a sequence to be prepared, adding nucleotide building blocks and an enzyme to generate nucleic acids that are complementary copies of the template sequences, and finally detaching the synthesized nucleic acids. In the presently claimed invention, the oligonucleotide that is immobilized to the support is the template. The template sequences remain bound and unchanged. This process can be repeated numerous times to produce numerous identical copies of the templates. Clearly the disclosure of Chetverin does not anticipate or render obvious the method recited in claim 1. Claims 3-7, and 9-31, depending from claim 1, are believed to be allowable for at least the above reasons. Thus, Applicants request that the rejection of claims 1, 3-7, and 9-31 be withdrawn.

With regard to claim 2, the Examiner referred to Figure 5B and column 4, lines 44-47 and column 6, lines 9-29 of Chetverin as anticipating a method for preparing a nucleic acid double strand. Applicants submit that Figure 5 appears to illustrate the generation of partial DNA fragment copies of a DNA parental strand on a 3' sectioned ordinary array. Figure 5A shows that the DNA is picked up from a particular well of the sorting array and spread on a partialing array. An unknown DNA parental strand 30 hybridizes to an oligonucleotide that is immobilized on the array, the oligonucleotide is then extended to produce a partial complementary copy of the parental strand, the array is vigorously washed to completely remove the parental strand 30, primers and polymerases are added to repeatedly produce copies of the template (see column 24, line 57 to column 25, line 28). Figure 5B only shows a method wherein a partial complementary copy of the parental strand is produced by extending the immobilized nucleotide after hybridization with the parental strand, washing away of the parental, and generation of 2 identical complementary copies (34 and 35) of the immobilized oligonucleotide. Chetverin discloses ligating the ends of the template strand and the produced strand together in the paragraph bridging columns 79 and 80. Applicants submit that claim 2 has been amended to recite "a method for preparing a predetermined nucleic acid double strand". In Chetverin, the copies of the added nucleic acid mixture that are produced are only partial copies of an unknown sequence of DNA. The presently claimed method is not anticipated by Chetverin for at least the reasons set forth above, and further, Applicants submit that the method of Chetverin has the disadvantage that the ultimate product is unknown before and after the copies are made. Thus, the user does not know what has been made by the method, and the

results are not reproducible. Clearly the disclosure of Chetverin does not anticipate or render obvious the method recited in claim 2. Claim 8, depending from claim 1, is believed to be allowable for at least the above reasons. Thus, Applicants request that the rejection of claims 2 and 8 be withdrawn.

New claims 32 and 33 have been added to define further embodiments of the invention. Support for these claims can be found in claims 20 and 21 as originally filed.

The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

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